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Investigating the Role of γ3, an Auxiliary Subunit of the BK Channel, in Myometrial Smooth Muscle Cells

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The large-conductance Ca^{2+}-activated K^+ (BK) channel is known to be important in regulating contractility and relaxation in myometrial smooth muscle cells (MSMCs) by controlling the flux of K^+ ions across the cell membrane. The BK channel is activated by voltage and intracellular Ca^{2+} concentration ($[Ca^{2+}]_{in}$). In addition, the BK channel has been shown to be constitutively active in MSMCs isolated from pregnant women during labor as compared to MSMCs isolated from non-laboring tissue. This underlying mechanism for this constitutive activity in BK activity has not been fully investigated. The BK channel can be modulated by auxiliary proteins, of which one type, the γ subunits, have been shown to activate the BK channel at relatively hyperpolarized membrane potentials and at very low $[Ca^{2+}]_{in}$. Here we studied whether association with the γ subunits could underlie the BK channel phenotype seen at labor. We focused on the γ3 subunit since it was reported to have the highest abundance in uterine smooth muscle. We investigated the expression and role of the γ3 subunit in non-laboring (NL) MSMCs using both molecular biology and electrophysiological techniques. Our first experiments assessed whether γ3 protein was present in hMSMCs, however we were unsuccessful due to the non-specificity of the antibodies targeted against γ3. To identify the functional role of the γ3 subunit, BK channel currents were measured using patch-clamp in the inside-out excised-patch configuration. We recorded currents from HEK cells overexpressed with BK channel alone and the BK channel co-expressed with the γ3 subunit, but did not detect a change in BK activity in the presence of the γ3 subunit. We also investigated whether the channel activity changed with a 1:4 ratio and from NL MSMC. Future studies will determine whether the association of the γ3 is present in laboring tissue.